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EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 12/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,520	LAL ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of group I, claims 1-6, SEQ ID NO:2, polynucleotide sequences encoding SEQ ID NO:1, and the species fragment of SEQ ID NO:3 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that 1) It would not be a burden for the Examiner to examine SEQ ID Nos:3-9, which are fragments of SEQ ID NO:2, and SEQ ID NO:10, which is a variant of SEQ ID NO:2, because these sequences would be found in a search for SEQ ID NO:2, 2) Groups II-VII, encompassing the methods of use of the polynucleotides of group I are classified in the same class and subclass, and have the same scope as the polynucleotides of group I, would therefore involve the same search and should be examined together with group I, and 3) The species requirement of groups VII and IX misrepresent the concept of election of species. The patentable distinctiveness of the molecules or compounds recited in the claims are not an issue for examination purposes as the claims are to a method of use of the composition of group I and not the species themselves.

This is not found persuasive because of the following reasons: 1) The species of SEQ ID Nos: 3-9 are structurally distinct from each other, and the variant of SEQ ID NO:10 is structurally distinct from SEQ ID NO:2 of group I. Thus their searches require different searches than the search for SEQ ID NO:2, and are not co-extensive, and it would be a serious burden for the Examiner to examine SEQ ID Nos:4-10 together with SEQ ID NOs:2, and 2) Although Groups III-VII are classified in the class and subclass, the searches for theses groups are complex, based on different database and not just on classification search, and are not co-extenisve, and therefore, it would be a serious

burden for the Examiner to examine these groups together. Further, Groups III-VIII are different from the polynucleotides of group I as product and process and are not of the same scope, and the searches for these groups are not co-extensive and therefore, it would be a serious burden for the Examiner to examine these groups together, and 3) In groups VII and IX, the species are used for combining with the polynucleotide of group I to detect specific binding. Since the species are structurally and functionally distinct, the methods of groups VII and IX, using different species, differ in reagents and/or dosages, and/or schedules used, response variables and criteria for success.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 1-6, SEQ ID NOs:2, 3 only are examined in the instant application. SEQ ID Nos: 4-9 are withdrawn from consideration as being drawn to non-elected species. SEQ ID NO:10 is withdrawn from consideration as being drawn to non-elected invention.

REJECTION UNDER 35 USC 101, UTILITY

35 U.S.C. 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claims 1-6 are drawn to 1) the nucleic acid sequence of SEQ ID NO:2, or a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:1, or complement thereof, 2) a fragment of SEQ ID NO:2, which is SEQ ID NO:3, 3) a vector comprising said nucleic acid sequence, a host cell comprising said vector, and 4) a method for using a cDNA to produce a protein.

The disclosed utilities for the polynucleotide of SEQ ID NO:2 encoding a STEAP related protein (STEAPRP) of SEQ ID NO:1, include diagnosis and treatment of cancer, in particular prostate hyperplasia and prostate cancer, production of and screening of antibodies that specifically bind to SEQ ID NO:1 (p.4-5). However, neither the specification nor any art of record teaches what SEQ ID NO:2 is, what it does do, they do not teach a utility for any of the fragments or the derivatives claimed, do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases. The asserted utilities for SEQ ID NO:2, such as production of and screening of agonists, antibodies and antagonists to the polypeptide of SEQ ID NO:1 encoded by SEQ ID NO:2 apply to many unrelated polypeptide structures sequences. Therefore the asserted utilities are not considered "specific" utilities, i.e. they are not specific to SEQ ID NO:2. Additional disclosed utilities for SEQ ID NO:2 include therapy and diagnosis of cancer, in particular prostate hyperplasia and prostate cancer. The asserted utility of SEQ ID NO:2 is based on the assertion that SEQ ID NO:1, encoded by SEQ ID NO:2 has chemical and structural homology to STEAP protein, a prostate specific marker (p.2), and that in particular SEQ ID NO:1 and STEAP protein share 43% identity (p.11). In addition, SEQ ID NO:1 has a biologically active portion extending from

T32 to L136 and several useful antigenic epitopes (p.11). Further, SEQ ID NO:1 has a potential N-glycosylation site, several potential phosphorylation sites, one potential KTN NAD binding domain, one potential bacterial-type phytoene dehydrogenase site, one potential oxidoreductase site, one potential phosphogluconate dehydrogenase site, one potential adrenodoxin reductase site , and six predicted transmembrane segments. The presence of these motifs indicates a possible function for STEAPRP in oxido-reductase reactions (p.10). By Northern analysis, SEQ ID NO:2 is overexpressed in prostate cancer cell line LNCaP as compared to PrEc non-tumerogenic prostate epithelial cells (p.10 and table 3 on p.41).

It is noted that the specification does not disclose any actual biological activity of SEQ ID NO:1, nor any data confirming that the portion extending from T32 to L136 of SEQ ID NO:1 has any biological activity, nor consensus sequences required for the activity of the encoded protein or for the identification of a STEAP protein. It is clear that, although there is a 43% identity between STEAP protein and SEQ ID NO:1, there is a 57% dissimilarity between SEQ ID NO:1 and STEAP protein; and the effects of these dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely

complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990) who teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252) who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Clearly, with 57% dissimilarity to STEAP protein, the function of the SEQ ID NO:1 could not be predicted, based on sequence similarity with STEAP, nor would it be expected to be the same as that of STEAP protein. In addition, Bork (Genome Research, 2000,10:398-400) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational

sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the errror rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrogngly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2). Further, Scott et al (Nature Genetics, 1999, 21:440-443) teach that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence

similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and 45% similarity to the human sulfate transporter downregulated in adenoma. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al. suggest that these results underscore the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph).

Clearly, given not only the teachings of Bowie et al, Lazar et al, Burgess et al and Scott et al, but also the limitations and pitfalls of using computational sequence analysis and the unknown effects of alternative splicing, post translational modification and cellular context on protein function as taught by Bork, with a 57% dissimilarity to STEAP protein, the function of the SEQ ID NO:1 could not be predicted, based on sequence similarity with STEAP protein, nor would it be expected to be the same as that of STEAP protein. Further, even if SEQ ID NO:1 is a STEAP-like protein, neither the specification nor any art of record teaches what the polypeptide is, what it does, does not teach a relationship to any specific disease or establish any involvement of the polypeptide in the etiology of any specific disease or teach which fragments might be active or which derivatives would function as claimed in a pharmaceutical composition.

Similarly, given the teachings of Bowie et al, Lazar et al, Burgess et al, Scott et al, and Bork, the function of the SEQ ID NO:1 could not be predicted, based on sequence similarity with a N-glycosylation site, phosphorylation sites, one KTN NAD binding domain, one bacterial-type phytoene dehydrogenase site, one oxidoreductase site, one phosphogluconate dehydrogenase site, and one adrenodoxin reductase site.

Moreover, although the specification discloses overexpression of SEQ ID NO:2 in a prostate cancer cell line LNCaP as compared to non-tumorigenic prosate epithelial cells PrEC, one cannot extrapolate data from cells in culture to those of primary prostate tumor cells. It is well known in the art that characteristics of cultured cell lines generally differ significantly from the characteristics of a primary tumor. Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded and that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the *bona fide* cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al (Immunol Ser, 1984, 23:181-207) specifically teaches that in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines and specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new artifactural antigens can occur as a result of culture (see attached abstract). Hsu (in

Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). The evidence presented clearly demonstrates that in cell culture systems, in general, and in cancer derived cell lines in particular, that artifactural chromosome constitutions and antigen expression are expected and must be taken into account when interpreting data received from cell line assays. Further, Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary - type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal

or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interations. Thus, based on the cell culture data presented in the specification, it could not be predicted that the cell lines LNCaP and PrEC could represent the parental, primary prostate hyperplasia or prostate cancer cells, and normal prostate epithelial cells, respectively, and that overexpression of SEQ ID NO:2 in the cell line LNCaP could be correlated with overexpression of SEQ ID NO:2 in primary prostate hyperplasia or prostate cancer.

Further, although the claimed polynucleotide of SEQ ID NO:2 is organ specific, i.e. specific to male reproductive tissue (table 1), its utilities based solely on prostate specific property, such as treating or detecting prostate cancer are not specific, and are shared by other unrelated prostate specific molecules.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

The following is a quotation of the first paragraph of 35 USC 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the written description inquiry, *whatever is now claimed.* (See page 1117). The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Claims 1-6 are drawn to a cDNA comprising 1) the nucleic acid sequence of SEQ ID NO:2, or a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:1, or a "complement" thereof, 2) a fragment of SEQ ID NO:2, which is SEQ ID NO:3, 3) a vector comprising said nucleic acid sequence, a host cell comprising said vector, and 4) a method for using a cDNA to produce a protein.

It is noted that a complement could be partial or complete complement, wherein partial complement could share with SEQ ID NO:2 only a few common nucleotides.

It is further noted that a CDNA "comprising" a fragment of SEQ ID NO:2 encompasses unrelated sequences that share with SEQ ID NO:2 a fragment of SEQ ID NO:2.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written description inquiry, *whatever is now claimed*. (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA..."requires a precise definition, such as by

structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention .

The instant specification fails to provide sufficient descriptive information, such as definitive strutural or functional features of the claimed genus of polynucleotides.

The claims 1-6 read on polynucleotide variants of SEQ ID NO:2, wherein said variants have any type of substitution besides conservative substitution, at any amino acid, throughout the length of the nucleic acid or peptide, as well as insertions and deletions. The specification and the claims do not place any limit on which amino acid that is subjected to conservative or non-conservative substitution, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. Thus the scope of the claims includes numerous structural polynucleotide variants, and nucleotide sequences encoding numerous structural variants. The specification and the claims do not provide any guidance as to which, or how many original amino acid(s) that are naturally substituted, or to which type of substitution besides conservative substitution, or which amino acids that are naturally deleted or inserted so that the claimed polypeptide could function as contemplated. Structural features, that could distinguish the claimed structural polynucleotide variants and nucleotide sequences encoding the polypeptide variants from the nucleotide sequences known in the art, are missing from the disclosure. No common structural attributes that identify the claimed structural polynucleotide variants and nucleotide sequences encoding the polypeptide variants are disclosed. In addition, no common functional attributes that identify the claimed structural polynucleotide variants and

nucleotide sequences encoding the polypeptide variants are disclosed, because the function of a nucleotide sequence could be abolished, even with substitution of only one amino acid of the peptide encoded by said nucleotide sequence (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138).

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of SEQ ID NO:2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. If Applicant could overcome the above 101 and 112, first paragraph rejection, claims 1, 4-6 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide of SEQ ID NO:2, does not reasonably provide enablement for a polynucleotide "encoding" SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 4-6 are drawn to a polynucleotide "encoding" SEQ ID NO:1, a vector comprising said polynucleotide, a host cell comprising said vector, and a method of making a protein.

The specification discloses isolation of SEQ ID NO:2 which is overexpressed in a prostate cancer cell line. There is no evidence that the deduced SEQ ID NO:1 is expressed in any tissue. One cannot extrapolate the teaching of the specification to the enablement of the claims because there is no teaching of whether any protein product is actually produced. Those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994,

page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and

translation. For the above reasons, one of skill in the art would not be able to predict if SEQ ID NO:2 is translated into a polypeptide expression product.

In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

2. If Applicant could overcome the above 101 and 112, first paragraph rejection, claims 1-6 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2, does not reasonably provide enablement for a "complement" of SEQ ID NO:2, or 3, or a complement of a nucleic acid sequence encoding SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-6 are drawn to 1) a complement of the nucleic acid sequence of SEQ ID NO:2, or of a fragment thereof of SEQ ID NO:3, or of a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:1, 2) a vector comprising said nucleic acid sequence, a host cell comprising said vector, and 3) a method for using a cDNA to produce a protein.

It is noted that a complement could be partial or complete complement, wherein partial complement could share with SEQ ID NO:2 only a few common nucleotides.

The claims encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to SEQ ID NO:2, that is polynucleotides that are complements of SEQ ID NO:2, or 3, or a nucleic acid sequence encoding SEQ ID NO:1. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a

variety of species including full-length cDNAs, genes and protein coding regions. Clearly, it would be expected that a substantial number of the hybridizing molecules encompassed by the claims **would not** share either structural or functional properties with SEQ ID NO:2.

In view of the above, one of skill in the art would be forced into undue experimentation in order to perform the claimed invention as broadly as claimed.

REJECTION UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 USC 102(b) as being anticipated by PN=6,329503, or Gattung et al, Genbank Sequence Database (Accession AC002064), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 1998 and 1997, respectively.

Claims 1-2 are drawn to a "complement" a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:1, or of the nucleic acid sequence of SEQ ID NO:2, or of a fragment of SEQ ID NO:2 which is SEQ ID NO:3.

PN=6,329503 teaches a polypeptide (SEQ ID NO:8) which is 100% similar to SEQ ID NO:1, from amino acid 246 to amino acid 418, according to sequence similarity search (MPSRCH search report, 2002, us-09-802-520-1.rai, page 1).

Gattung et al teach a polynucleotide, which is 99.8% similar to SEQ ID NO:2, from nucleotide number 804 to 1338, according to sequence similarity search (MPSRCH search report, 2002, us-09-802-520-2.rge, pages 2-4), and a polynucleotide sequence which is 99.6% similar to SEQ ID NO:3, from nucleotide number 280 to 508, according to sequence similarity search (MPSRCH search report, 2002, us-09-802-520-3.rge, pages 2-3).

Given the polypeptide taught by PN=6,329503 and the polynucleotide sequences taught by Gattung et al, one of ordinary skill in the art would immediately envision the claimed polynucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

November 10, 2002

SUSAN UNGAR
PRIMARY EXAMINER

SUSAN UNGAR, PH.D
PRIMARY EXAMINER